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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WILSON, MICHAEL C	

ART UNIT	PAPER NUMBER
1632	

NOTIFICATION DATE	DELIVERY MODE
09/18/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

nyuspatactions@ladas.com

Office Action Summary	Application No.	Applicant(s)	
	10/585,623	CHEN, FENGLIN	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 14-22* is/are pending in the application.

4a) Of the above claim(s) *1-10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9-7-06&5-30-07&6-14-07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 6-8-09 is missing claim 13. This office action is being set forth to expedite prosecution but the proper response to the amendment should have been a "Non-responsive amendment" letter. Applicants acknowledge claims 11-13 have been canceled in the first line of the response filed 6-8-09. It is assumed claim 13 has been canceled. Please confirm this in your next response by including claim 13 with the status identifier: Canceled.

Claim Objections

Claim 14 is objected to because the phrase "subject in need of treatment" in the body of the claim is not the same scope as "subject with recurrent spontaneous abortion" in the preamble. Use of "subject with recurrent spontaneous abortion" in the body of the claim is preferred. It would also be acceptable to simply refer to "the subject," i.e. administering to said subject a therapeutically effective...."

The phrase "fibronectin encoding gene" can be more clearly written --fibronectin gene.—

If applicants intend the chromosome 2 in claim 14 to be obtained from a male, the claim should be more clearly written, i.e. --chromosome No. 2 or fragment thereof containing a fibronectin gene, wherein said chromosome No. 2 or fragment thereof is obtained from a male mate of the subject.

Election/Restrictions

Applicant's election with traverse of Group III, claims 13-22, in the reply filed on 6-8-09 is acknowledged. Since claim 13 has been canceled, it is assumed applicants

were merely referring to the original claims in Group III. The traversal is on the ground(s) that the chromosome No. 2 or fragment thereof derived from a male is required in both Groups I and III. This is not found persuasive. Inventions I and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the chromosome or fragment thereof containing a fibronectin gene in Group I can simply be used to express fibronectin in vitro and the method of Group III can be performed with a fibronectin gene from a female or with a chromosome or fragment thereof from any male (not necessarily the mate). The search required for the product in Group I does not require the search for the method of Group III. The requirement is still deemed proper and is therefore made FINAL.

Claims 1-10 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 11-13 have been canceled. Applicant timely traversed the restriction (election) requirement in the reply filed on 6-8-09.

Claims 14-22 are under consideration. Claim 13 has been canceled.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 14 is drawn to a method of treating a subject with recurrent spontaneous abortion comprising administering to a subject in need of treatment a therapeutically effective amount of chromosome No. 2 or fragment thereof containing fibronectin encoding gene obtained from a male mate of said subject.

Claim 17 is drawn to a method of treating a subject with recurrent spontaneous abortion comprising administering to a subject in need of treatment a therapeutically effective amount of chromosome No. 2 or fragment thereof containing fibronectin encoding gene obtained from a plurality of males.

Claims 14 and 17 encompass treating subjects with recurrent spontaneous abortion (RSA) with chromosome 2 or a fragment thereof containing a fibronectin gene. Chromosome 2 encompasses different chromosomes in different species because the number of chromosomes in each species varies. The claims encompass administering the chromosome alone – in the absence of cells. The claims also encompass administering any chromosome 2 from any species that contains a fibronectin gene obtained from a male mate. The claims encompass administering chromosome 2 from any male mate that contains a fibronectin gene or administering chromosome 2 from male or female comprising a fibronectin gene obtained from a male mate. The fragment

thereof comprising a fibronectin gene obtained from a male mate encompasses a chromosome 2 obtained from a male mate into which the fibronectin gene has been inserted or fibronectin gene obtained from chromosome 2 of a male mate. The phrase male mate encompasses a male that can mate with the subject and males that have mated with the subject.

The art at the time taught RSA was two or more consecutive spontaneous abortions (pg 1 last 3 lines). RSA can be the result of many causes including abnormal chromosomes, endocrine imbalance, anatomical abnormality of reproductive organs, bacterial or viral infection, blood group incompatibility. RSA can also have an unknown cause; immunological factors are thought to be the cause of unexplained RSA. RSAs associated with immunological factors are called immunological RSAs (pg 2, lines 8-19). The immunological factors that may affect RSA include blocking antibodies, e.g. anti-paternal cytotoxic antibodies (APCA), anti-idiotype antibodies (Ab2) and mixed lymphocyte reaction blocking antibodies (MLR-Bf) which can inhibit the attack to fetus by the maternal immune system.

No method of treatment with definite curative effect is available heretofore (pg 3, lines 3-4 of second paragraph). Lymphocyte immunotherapy is used to treat immunological RSA which is an intracutaneous infusion of mixed leukocytes derived from the subject's spouse (pg 3 end of second paragraph; pg 4, lines 1-2). However, this therapy is not definite and treatment showed no difference as compared to a control (pg 4, last 8 lines; pg 5, lines 1-7).

The specification teaches patients with early secondary RSA had no fibronectin band between the trophoblast and caduca as compared to control samples (pg 21, Example 1). A mixture of chromosome 2 derived from a plurality of men (generally more than 20) was prepared. Patients' serum was added to the chromosomes and mouse anti-human IgG antibody was added to mixture. The results of the assay are not disclosed but appear to relate to determining which patients are eligible for treatment, i.e. those that have increased specific antinuclear antibodies in their serum (pg 21-23, Example 2). Venous blood was taken from the spouse of a patient, and lymphocytes were cultured and isolated. The lymphocytes were lysed (pg 24, item (4)), and a suspension made from the lysate was injected subcutaneously to the patient. The specification does not teach isolating chromosome 2 from the lysate, that the lysate has intact chromosome 2 or that the lysate has any intact chromosome (pg 23-25, Example 3). The suspension was administered to the patient four times and the patient had a baby (pg 26, Example 4; pg 27, Example 5). The treatment was used on 300 patients that had early secondary RSA, increased level of specific antinuclear antibody in peripheral blood (>1:64) with a rate of >95% (pg 28, Example 6).

The patent office does not have the ability to determine the final suspension that is administered to the patient. It is recognized that the lymphocytes of the spouse are lysed and that a suspension is made from the contents of the cells but the specification does not teach isolating chromosome 2 from the lysate, that the lysate has intact chromosome 2 or that the lysate has any intact chromosome. The structure of the final suspension injected into the patient is wholly unclear. Clarification is required.

The claims encompass administering only a male chromosome 2 containing a fibronectin gene. The specification and the art at the time of filing do not teach the patient's immune response against the male chromosome 2 alone would be adequate to prevent RSA. It appears that all the male chromosomes are part of the lysate made in the final suspension described by applicants (Example 3). Without correlating the lysate made in the final suspension described by applicants to administering the single male chromosome 2 comprising a fibronectin gene, it would have required those of skill undue experimentation to treat RSA using the male chromosome 2 alone as encompassed by the claims.

The claims encompass administering intact, condensed, male chromosomes comprising chromosome 2 comprising a fibronectin gene. Claims 15, 18 specifically require administering intact chromosome 2. The claims encompass administering an intact, condensed set of male chromosomes or intact, condensed male chromosome 2 alone to the patient. The specification and the art at the time of filing do not teach the patient's immune response against a full set of intact, condensed, male chromosomes would be adequate to prevent RSA. The specification and the art at the time of filing do not teach the patient's immune response against an intact, condensed, male chromosome 2 would be adequate to prevent RSA. In particular, it is not readily apparent that the patient's immune response could recognize the proper regions of the chromosomes when they are intact and condensed. To the contrary, it appears that all the male genomic DNA is part of the lysate made in the final suspension described by applicants (Example 3); it is not readily apparent that the chromosomes are intact or

that the immune system could generate antibodies against any part of the DNA being administered. Without correlating the lysate made in the final suspension described by applicants to administering intact, condensed male chromosomes comprising chromosome 2, it would have required those of skill undue experimentation to treat RSA using intact, condensed male chromosomes comprising chromosome 2 as encompassed by the claims.

The claims encompass administering a fragment of a male chromosome 2 comprising a fibronectin gene; this encompasses administering only a fibronectin gene isolated from male chromosome 2. The specification and the art at the time of filing do not teach the patient's immune response against a fibronectin gene isolated from the male chromosome 2 alone would be adequate to prevent RSA. It appears that the entire male genomic DNA is part of the lysate made in the final suspension described by applicants (Example 3). Without correlating the lysate made in the final suspension described by applicants to administering a fibronectin gene isolated from male chromosome 2, it would have required those of skill undue experimentation to treat RSA using a fibronectin gene isolated from the male chromosome 2 alone as encompassed by the claims.

The specification does not enable treating any patient with RSA using a suspension made by the process described in Example 3. The specification and the art at the time of filing do not teach how to use an immunological treatment as claimed when RSA is caused by abnormal chromosomes, endocrine imbalance, anatomical abnormality of reproductive organs, bacterial or viral infection, blood group

incompatibility. The specification and the art at the time of filing are limited to treating immunological RSA (pg 2, lines 8-19). More specifically, the invention appears to require the patient has increased specific antinuclear antibodies in their serum greater than 1:64 (pg 21-23, Example 2; pg 28, line 4). Without correlating the RSA patients with increased specific antinuclear antibodies in their serum greater than 1:64 to RSA patients caused by other problems, it would have required those of skill undue experimentation to determine how to use the invention to treat a patient with any type of RSA as broadly claimed. Accordingly, the claims should be limited to treating RSA patients having increased specific antinuclear antibodies in their serum greater than 1:64.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 15 and 18 are indefinite because it is unclear how the claims further limits claim 14 or 17. It is unclear if applicants intend the claim to limit the "chromosome No. 2 or fragment thereof" in claim 14 or 17 to the "chromosome No. 2" and exclude the "fragment thereof" or if applicants are attempting to further limit the structure of the "chromosome No. 2 or fragment thereof". The claim does not clearly refer back to the structure being administered in claim 14 or 17.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 14 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Gatenby (Am. J. Reprod. Immunol., 1993, Vol. 29, No. 2, pg 88-94).

Gatenby administered lymphocytes from a male mate of a patient with RSA (pg 3, last 10 lines, of the specification). The lymphocytes inherently had intact male chromosome 2 comprising a fibronectin gene as claimed because the fibronectin gene is part of chromosome 2 and the entire genome of the cells was introduced to the patient.

Conclusion

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within

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If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

/Michael C. Wilson/
Primary Patent Examiner